Chronic stress and intestinal barrier function

Implications for infection and inflammation in intensive salmon aquaculture

Akademisk Avhandling

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Dissertation Abstract

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Aquaculture is a fast growing food-producing sector worldwide. This has increased the awareness among the public as well as governments of the need to secure the welfare and health of farmed fish. Atlantic salmon is, in non-Asian countries, one of the most successful aquacultured species. Despite continuous improvement of husbandry practices and development of new vaccines, both bacterial and viral diseases are main threats to the health of farmed Atlantic salmon. Chronic stress, created by sub- optimal husbandry conditions is believed to be an important factor behind disease outbreaks. The intestinal epithelium of Atlantic salmon is an important organ. Not just in nutrient absorption, but also as a barrier, preventing antigens and pathogens within the intestinal lumen to gain entrance to the host and thereby start an infection. Chronic stress is known to have a negative impact on the intestinal barrier in mammals, a situation that can cause a leaky epithelium and increased bacterial translocation. Stressful husbandry conditions could have a similar effect on the intestine of Atlantic salmon and would thus be a major threat to the welfare of farmed fish.

This thesis aimed at elucidating the importance of the intestinal physical and immunological barrier function in disease susceptibility of farmed Atlantic salmon. It further aimed to reveal the impact of key husbandry conditions in Atlantic salmon aquaculture hypothesized to be potential threats to health and welfare of the fish.

All husbandry conditions examined, *i.e.* hyperoxygenation combined with low water flow, low levels of dissolved oxygen and high temperature as well as high fish density in combination with poor water quality was concluded stressful to the fish. These common husbandry practises all generated primary and secondary stress responses such as increased plasma cortisol levels, increased cortisol release rate into the water and a decreased function of all intestinal barriers. Decreased physical barrier was evident in the form of increased paracellular permeability. This was accompanied by increased translocation rates of the pathogen bacteria *Aeromonas salmonicida*, suggesting an increased risk for bacterial infections in fish under chronic stress. Dysfunction of the intestinal immunological barrier was manifested as impaired expression of the pro-inflammatory cytokine IFN-γ. This down regulation could be the result of an immune-suppressive effect of cortisol but could also be an effect of the decreased physical intestinal barrier resulting in increased leakage of luminal antigens. The decreased expression of IFN-γ could be a sign of decreased cellular immunity which would render an intestinal barrier with reduced ability to cope with virus infections like the IPNV. Chronic stress also resulted in increased homing of neutrophils and signs of sever local inflammation. These findings suggest that stressed fish may experience increased disease susceptibility towards viral pathogens like IPNV as well as an increased risk of developing chronic intestinal inflammation.

Intestinal barrier function was further evaluated as a new scientific tool for assessment of potential threats to welfare in aquaculture. The intestine was demonstrated to be a sensitive indicator of stress at times when no or only minor differences in primary stress responses was observed

In conclusion, common husbandry may constitute a threat to health and welfare of farmed fish and intestinal barrier function can serve as a valuable tool for assessing potential stressful husbandry conditions in the future.

Keywords: Intestinal barrier function, stress, cortisol, Ussing chambers, welfare, health, inflammation, neutrophils, cytokines, chronic stress, chronic inflammation